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On _____

TOWNSEND and TOWNSEND and CREW LLP

By: _____

PATENT
Docket No.: 026549-000100US
Client Ref. No.: 30836

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No.: 1519
Ronit Eisenberg	Examiner: Crowder, Chun
Patent No.:	Art Unit: 1644
Issued:	RULE 132 DECLARATION
Application No.: 10/009,809	
Filed: April 26, 2002	
For: CELL PENETRATING ANTI-ALLERGIC PEPTIDES	

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Dr. Ronit Sagi-Eisenberg, being duly warned that willful false statements and the like are punishable by fine or imprisonment or both, under 18 U.S.C. § 1001, and may jeopardize the validity of the patent application or any patent issuing thereon, state and declare as follows:

1. All statements herein made of my own knowledge are true and statements made on information or belief are believed to be true. **The Exhibits (1 and _ attached hereto are incorporated herein by reference.**

2. I received a Ph.D. in Biochemistry from the University of Tel Aviv in 1980.

A copy of my curriculum vitae is attached as Exhibit 1.

3. I am presently employed at Tel Aviv University and am primarily responsible for teaching and research.

4. I have read and am familiar with the contents of the application. I understand that the Examiner has a single rejection based on obviousness that is based on a combination of three references. The references are Holgate as a primary reference in view of Aridor and Lin. Holgate is cited as disclosing that agents that inhibit mast cell degranulation are recognized for treatment of diseases such as asthma. Aridor discloses KNNLKECGLY which is a mast cell activation inhibitor designated Gαi3 C-terminal peptide. Lin discloses the preferred cell penetrating peptide from Kaposi fibroblast growth factor [KFGF].

5. This invention is the surprising discovery that of four different cell penetrating peptides (CCP) only one CCP was able to successfully deliver two mast cell activation inhibitors in a biologically active manner. Because the prior art literature would suggest to those of skill that CCPs are interchangeable, it is surprising that the choice of CCP would be critical for obtaining biological activity. Accordingly, we have to conclude that the field of using cell penetrating peptides to deliver biologically active proteins is far less predictable than the Examiner believes it to be and that the applicants' results as embodied in the pending claims are both surprising and advantageous.

The following statements provide objective, scientific reasons for the above conclusion.

6. It is my understanding that the rejection of the pending claims is based on the proposition that Lin's teaching of the CCP, (AAVALLPAVLLALLAP) as a tool for delivery of biologically active cargo peptides renders the claimed combinations of AAVALLPAVLLALLAP in reading frame fusions with $G\alpha i_3$ or Gαt C-terminal peptides obvious and unpatentable. In brief, the Examiner believes that upon reading the three references, one of skill would be motivated by Holgate to combine the KFGF CCP of Lin with the mast cell activation inhibitor of Aridor, $G\alpha i_3$, with a reasonable expectation that the combination would inhibit mast cell activation.

It is also my understanding that evidence of unpredictability or surprising results can legally refute this conclusion and lead to the rejection being withdrawn.

It is my further opinion that both unpredictability and surprising results have been demonstrated by the applicants' work and by the literature already of record.

7. More specifically, we know that of the four CCPs tested only one CCP was able to deliver the two mast cell activation inhibitors, $G\alpha i_3$ or Gαt, as a biologically active inhibitors. The table below summarizes Applicants' results as described in the specification and in the Jones et al. publication.

CHIMERIC PEPTIDE			RESULTS
Hu Int	$G\alpha i_3$	SEQ ID NO: 6	No inhibition of histamine secretion
KFGF	$G\alpha i_3$	SEQ ID NO: 7	**Inhibited histamine secretion**
Dros	$G\alpha i_3$	SEQ ID NO: 10	Induced histamine

			secretion
Hu Int	Gαt	SEQ ID NO: 11	No inhibition of histamine secretion
KFGF SEQ ID NO: 3	Gαt	SEQ ID NO: 12	**Inhibited histamine secretion**
Dros	Gαt	SEQ ID NO: 13	Induced histamine secretion
TP-10	$G\alpha i_3$	Jones *et al.*	No inhibition of beta-hexoseaminidase secretion

8. From this data, it is clear that only Lin's CCP, KFGF is able to both deliver mast cell activation inhibitors and maintain their biological activity as inhibitors of mast cell activation . The Examiner says that this is predictable from the literature. I respectfully disagree.

Lin discloses that KFGF sequence transported two biologically active cargo peptides and generally states that KFGF can be used to transport other peptides. But similar reports exist for each of the other CCPs tested by applicants. The Hawiger review article discloses that the CCP designated integrin β_3 is just as able as KFGF to transport functional peptides into a cell (see page 189, 2nd column). Finally Derossi *et al.* describes the *Drosophila* CCP as successfully delivering biologically active compounds inside live cells (page 18188, 2nd col).

From page 7 of the Office Action, the Examiner appears to interpret this literature as leading one of skill to believe that there is a reasonable expectation that any

combination of CCP with any biologically active peptide will lead to the observation of biological activity in a cell.

I respectfully disagree. There are several scientific and objective reasons why fusing a CCP to a biologically active peptide might not result in observation of expected biological activity. These reasons include improper folding of the fusion peptide resulting in conformational changes that render the cargo peptide inactive; the degradation of the foreign peptide; sequestering of the peptide a endosomes or the ability of the CCP sequence to trigger a biological response, such as mast cell degranulation (e.g. positively charged CCP might function as basic secretagogues of mast cells).

Indeed, this appears to be the case for fusion of CCP with either $G\alpha i_3$ or $G\alpha t$. The data from applicants' laboratory and from the Jones *et al.* group demonstrate that not any CCP can maintain the biological activity of $G\alpha i_3$ or $G\alpha t$. Of four CCPs, only KFGF was the only CCP able to both internalize and maintain the inhibitory activity of both $G\alpha i_3$ and $G\alpha t$. Thus the combination provides a surprisingly advantageous result that was not predictable from the prior art.

I do note the Examiner's statement on page 7 that the table on page 9 with reference to the prior literature describing the various CCPs fail to demonstrate that Lin's CCP is unpredictable as a delivery tool. While this is true, there was no academic reason *a priori* to believe that any of the other CCPs would fail to deliver $G\alpha i_3$ and $G\alpha t$ while maintaining its expected biologically activity. But the evidence established by the record indicates that this is not true. There is obviously something special about the two mast cell activation inhibitors or with Lin's CCP that makes the claimed combination functional compared to the other three CCPs.

For these reasons, I conclude without hesitation that the claimed combinations of AAVALLPAVLLALLAP with either $G\alpha_{i3}$ or $G\alpha t$ to yield a functional inhibitory effect on mast cell activation in light of failure with three other CCPs of equal status was unpredictable, surprising and of great value.

This Declarant has nothing further to say.

Dated: May 6 2007

Dr. Ronit Sagi-Eisenberg

Ronit Sagi-Eisenberg

CURRICULUM VITAE

NAME	**Ronit**	**Sagi-Eisenberg**
	First	Last
	Ph.D.	
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MARITAL STATUS	**Widow**
NO. OF CHILDREN	**3**
	status children

A. EDUCATION

PERIOD OF STUDY (DATES)	
1970 - 1973	**Tel Aviv University, Tel Aviv, Israel** **Chemistry** (Subject) **B.Sc.** (Degree) **1974** (Date Awarded)
1974 - 1975	**Tel Aviv University, Tel Aviv, Israel** **Biochemistry** (Subject) **M.Sc. studies-upgraded to Ph.D.**
1975-1980	**Tel Aviv University, Tel Aviv, Israel** **Bioenergetics** (Subject) **Ph.D.** (Degree)
Title of Doctoral Dissertation	Kinetic and energetic aspects of the Q cycle model.
Names of Supervisors	Name **Menachem Gutman** Title **Professor Emeritus**

B. ACADEMIC AND PROFESSIONAL EXPERIENCE	
PERIOD (DATES)	
1975-1980	**Tel Aviv University, Tel Aviv, Israel** **Chemistry** (Subject) **Biochemistry** (Department) **Teaching Assistant** (Rank/Function)
1980-1984	**The Weizmann Institute of Science, Rehovot, Israel.** **Mast cell biology** (Subject) **Chemical Immunology** (Department) **Post Doctoral fellow at the laboratory of Prof. I. Pecht.** (Rank/Function)
08/82-11/82 08/83-11/83	**University College London, London, U.K** **Mast cell biology** (Subject) **Pharmacology** (Department) **Honorary Research Assistant at the laboratory of Prof. J. Foreman.** (Rank/Function)
1984-1985	**The Weizmann Institute of Science, Rehovot, Israel.** **Mast cell biology** (Subject) **Chemical Immunology** (Department) **Investigator** (Rank/Function)
1985-1989	**The Weizmann Institute of Science, Rehovot, Israel.** **Signaling mechanisms underlying mast cell exocytosis.** (Subject) **Chemical Immunology** (Department) **Senior Investigator** (Rank/Function)
1989-1991	**The Weizmann Institute of Science, Rehovot, Israel.** **Signaling mechanisms underlying mast cell exocytosis.** (Subject) **Chemical Immunology**

	(Department) **Associate Professor** (Rank/Function)
1991-1994	**National Institutes of Health, Bethesda, MD, USA** **Mast cell exocytosis.** (Subject) **Laboratory of Chemical Pharmacology** (Department) **Visiting scientist at the Laboratory of Dr. Michael Beaven** (Rank/Function)
1994-present	**Tel Aviv University, Tel Aviv, Israel** **The interplay between trafficking and signaling; clinical applications.** (Subject) **Cell and Developmental Biology** (Department) **Associate Professor** (Rank/Function)

C. MEMBERSHIP IN PROFESSIONAL SOCIETIES	
Year	Society
1985-1991	The Israel Biochemical Society
1994-present	The Israel Society for Cell Biology
1997	The American Society of General Physiologists.

D. ADMINISTRATIVE DUTIES	
1995-1999	Member of the Animal Care and Use Committee
1996-1999	Treasurer of the Israel Society for Cell Biology
1997-2001	Preclinical Advisor for the Sackler School of Medicine, New York State/American Program
1998-2001	Member of the Teaching Committee of the Sackler School of Medicine, New York State/American Program
1998-present	Member of the Research and Development Committee of the Sackler Faculty of Medicine.
1998-2006	Head of the Sackler Faculty of Medicine Committee for Laboratory Space
1998-2006	Member of the Search Committee of the Sackler Faculty of Medicine
1999-present	Head of Admission Committee, Graduate program, Occupational Therapy
2002-present	Member of the Teaching Committee of the School of Continuing Medical Education
2002-2006	Member of the Ph.D. students committee

2002-present	Member of the University Committee of Intellectual property.
2005-present	Head of the Dept. of Cell and Developmental Biology,
2006- present	Member of the Sackler Faculty of Medicine committee for Scholarships.
2006-present	Member of the Sackler Faculty of Medicine board.
2006-present	Head of the Dr. Miriam and Sheldon G. Adelson Gradu School of Medicine.

E. FIELDS OF INTEREST
Signal Transduction, Protein Traffic, Allergic and Inflammatory diseases, Cancer

SCIENTIFIC PUBLICATIONS

A. ORIGINAL ARTICLES

A.1 Articles Published

1. **Sagi-Eisenberg, R.** and Gutman, M.
"Generation of high $\Delta\Psi$ in Respiring Submitochondrial Particles by Steady-State Accumulation of Oxidized N,N,N',N' - Tetramethyl-p-phenylenediamine".
Eur. J. Biochem. **97**, 127-132 (1979).
2. **Sagi-Eisenberg, R.** and Gutman, M.
"Rate Limiting Step in Oxidation of Physiological and Artificial Reductants by Azotobacter Vinelandii Membrane Vesicles".
Arch. Biochem. Biophys. **197**, 470-476 (1979).
3. **Sagi-Eisenberg, R.**, Ben-Neriah, Z., Pecht I., Terry S. and Blumberg S.
"Structure Activity Relationship in the Mast Cell Degranulating Capacity of Neurotensin Fragments".
Neuropharmacology **22**, 197-201 (1983).
4. **Sagi-Eisenberg, R.** and Pecht, I.
"Membrane Potential Changes During IgE-Mediated Histamine Release from Rat Basophilic Leukemia Cells (RBL)".
J. Memb. Biol. **75**, 97-104 (1983).
5. **Sagi-Eisenberg R.**, Geller-Bernstein C., Ben-Neriah Z. and Pecht I.
"Direct Measurement of the Dextran-Dependent Calcium Uptake by Rat Peritoneal Mast Cells".
FEBS Lett. **161**, 37-40 (1983).
6. **Sagi-Eisenberg, R.** and Pecht, I.
"Resolution of Cellular Compartments Involved in Membrane Potential Changes Accompanying IgE-Mediated Degranulation of Rat Basophilic Leukemia Cells".
EMBO J. **3**, 497-500 (1984).
7. **Sagi-Eisenberg, R.** and Foreman, J.C.
"Fractionation of Mast Cell Components for studies of Ligand-Receptor Binding at the Plasma Membrane".
Immunol. Lett. **8**, 43-47 (1984).
8. **Sagi-Eisenberg, R.** and Pecht, I.
"Protein Kinase C, a Coupling Element between Stimulus and Secretion in Basophils".
Immunol. Lett. **8**, 237-241 (1984).
9. **Sagi-Eisenberg, R.**, Mazurek, N. and Pecht, I.
"Ca^{2+} Fluxes and Protein Phosphorylation in Stimulus-Secretion Coupling of Basophils".
Molec. Immunol. **21**, 1175-1181 (1984).
10. **Sagi-Eisenberg, R.**
"A Possible Role for a Calcium Activated, Phospholipid Dependent Protein Kinase in the Mode of Action of the Anti-Allergic Drug Disodium Cromoglycate".
Trends Pharmacol. Sci. **6**, 198-201 (1985).
11. **Sagi-Eisenberg, R.**, Lieman H. and Pecht I.

"Protein Kinase C Regulation of the Receptor Coupled Calcium Signal in Histamine Secreting Rat Basophilic Leukemia Cells".
Nature **313**, 59-60 (1985).

12. **Sagi-Eisenberg, R.**, Foreman, J.C. and Shelly, R.
"Histamine release induced by histone and phorbol ester from rat peritoneal mast cells".
Eur. J. Pharmacol. **113**, 11-17 (1985).

13. Tarrab-Hazdai, R., **Sagi-Eisenberg, R.**, Brenner, V. and Arnon, R.
"Ion fluxes changes during early stages of Schistosoma mansoni; Evaluation of complement effect".
Eur. J. Biochem. **154**, 563-568 (1986).

14. Zick, Y., **Sagi-Eisenberg, R.**, Pines, M., Gierschik, P. and Spiegel, A.M.
"Multi-site phosphorylation of the alpha subunit of transducin by the insulin receptor kinase and protein kinase C".
Proc. Natl. Acad.Sci. USA, **83**, 9294-9297 (1986).

15. Reck, B., **Sagi-Eisenberg, R.** and Pecht, I.
"Cytosolic free Ca^{2+} in mast cells and their mediators release".
J. Allergy Clin. Immunol., 164-169 (1986).

16. **Sagi-Eisenberg, R.**, Foreman, J.C., Raval, P.J. and Cockcroft, S.
"Protein and diacylglycerol phosphorylation in the stimulus secretion coupling of rat mast cells."
Immunology, **61**, 203-206 (1987).

17. Zick, Y., Spiegel, A.M. and **Sagi-Eisenberg, R.**
"Insulin-like growth factor I receptors in retinal rod outer segments".
J. Biol. Chem. **262**, 10259-10264 (1987).

18. Safran, A., **Sagi-Eisenberg, R.**, Neuman D. and Fuchs S.
"Phosphorylation of the acetylcholine receptor by protein kinase C and identification of the phosphorylation site within the receptor d-subunit".
J. Biol. Chem. **262**, 10506-10512 (1987).

19. **Sagi-Eisenberg, R.**
"GTP-binding proteins as possible targets for protein kinase C action.
Trends Biochem. Sci. **14**, 355-357 (1989).

20. **Sagi-Eisenberg, R.**, Traub, L.M., Spiegel, A.M. and Zick, Y.
"Protein kinase C mediated phosphorylation of retinal rod outer segment membrane proteins".
Cell. Signalling **1**, 519-531 (1989).

21. Safran, A., Provenzano, C., **Sagi-Eisenberg, R.** and Fuchs, S.
"Phosphorylation of membrane-bound acetylcholine receptor by cAMP-dependent protein kinase and protein kinase C; Characterization and subunit specificity".
Biochemistry **29**, 6730-6734 (1990).

22. Gat-Yablonski, G. and **Sagi-Eisenberg, R.**
"Evaluation of the role of inositol trisphosphate in IgE-dependent exocytosis".
Biochem. J. **270**, 685-689 (1990).

23. Gat-Yablosnki, G. and **Sagi-Eisenberg, R.**
"Differential down-regulation of protein kinase C selectively affects IgE-dependent exocytosis and inositol trisphosphate formation".
Biochem. J. **270**, 679-684 (1990).

24. Aridor, M., Traub, L. and **Sagi-Eisenberg R.**

"Exocytosis in mast cells by basic secretagogues; Evidence for direct activation of GTP-binding proteins".
J. Cell Biol. **111**, 909-917 (1990).

25. Traub, L.M., Evans, H.W. and **Sagi-Eisenberg, R.**
"A novel 100 kDa protein, localized to receptor enriched endosomes, is immunologically related to the signal transducing G proteins Gt and Gi."
Biochem J., **272**, 453-458 (1990).

26. Zick, Y. and **Sagi-Eisenberg, R.**
"A combination of H_2O_2 and vanadate concomitantly stimulates protein tyrosine phosphorylation and polyphosphoinositide breakdown in different cell lines".
Biochemistry **29**, 10240-10245 (1990).

27. Aridor, M. and **Sagi-Eisenberg, R.** "Neomycin is a potent secretagogue of mast cells that directly activates a GTP-binding protein involved in exocytosis".
J. Cell Biol. **111**, 2885-2891 (1990).

28. Traub, L.M., Shai, E. and **Sagi-Eisenberg, R.**
"Characterization of the interaction between p100, a novel G protein-related protein, and rat liver endosomes".
Biochem J. **280**, 171-178 (1991).

29. Traub, L.M., and **Sagi-Eisenberg, R.**
"Purification of p100, a protein antigenically related to the signal transducing G proteins Gt and Gi; Evidence for an adaptin like protein".
J. Biol. Chem. **266**, 24642-24649 (1991).

30. Hulkower, K.I., **Sagi-Eisenberg, R.**, Traub, L.M., Georgescu, H.I. and Evans, C.H. " Interleukin-1 and synovial protein kinase C: Identification of a novel, 35kDa cytosolic substrate".
Agents and Actions **34**, 278-281 (1991).

31. Hulkower, K.I., **Sagi-Eisenberg, R.**, Traub, L.M., Georgescu, H.I. and Evans, C.H.
" Synovial protein kinase C and its apparent insensitivity to interleukin-1".
Eur.J. Biochem. **209**, 81-88 (1992).

32. Aridor, M., Rajmilevich, G., Beaven, M. and **Sagi-Eisenberg, R.**
"Activation of exocytosis by the heterotrimeric G-protein Gi3 "
Science. **262**, 1569-1572 (1993).

33. Hydar, A., Maeyama, K., **Sagi-Eisenberg, R.** and Beaven, M.A.
"Antigen and Thapsigargin promote influx of Ca^{2+} in rat basophilic RBL-2H3 cells by ostensibly similar mechanisms that allow filling of inositol 1,4,5-trisphosphate-senesitive and mitochondrial Ca^{2+} stores".
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34. Kassessinoff, T.A., Gabet, A., Beaven, M.A. and **Sagi-Eisenberg, R.**
"Inositol polyphosphates regulate the membrane interactions of the endosomal p100, G-Protein-related protein".
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35. Baram, D., Linial, M., Mekori, Y.A. and **Sagi-Eisenberg, R.**
" Ca^{2+}- dependent exocytosis in mast cells is regulated by the Ca^{2+} sensor Synaptotagmin I".
J. Immunol. (Cutting Edge) **161**, 5120-5123 (1998). (Immunology 12/115 IF 6.39)

36. Shefler, I., Taube, Z., Medalia, O. and **Sagi-Eisenberg, R.**
"Basic secretagogues activate protein tyrosine phosphorylation and release of arachidonic acid

in mast cells via a novel protein kinase C and phosphatidylinositol 3-kinase-dependent mechanism"
Eur. J. Immunol. **28**, 3468-3478 (1998). (Immunology 16/115 IF 4.88)
37. Zussman, A., Hermuet, S. and **Sagi-Eisenberg, R.**
"Stimulation of Ca^{2+}-dependent exocytosis and arachidonic acid release in cultured mast cells (RBL-2H3) by a GTPase-deficient mutant of Gαi3."
Eur. J. Biochem. **258**, 144-149 (1998). (Biochemistry 92/261 IF 3.16).
38. Shefler, I., Seger, R. and **Sagi-Eisenberg, R.**
"Gi-mediated activation of the mitogen-activated protein kinase (MAPK) pathway by the receptor mimetic basic secretagogues of connective tissue type mast cells. Bifurcation of arachidonic acid-induced release upstream of MAPK."
J. Pharmacol. Exp. Ther. **289**, 1654-1661 (1999). (Pharmacology 26/193 IF 4.1)
39. Baram, D., Adachi, R., Medalia, O., Tuvim, M., Dickey, B.F., Mekori, Y.A. and **Sagi-Eisenberg, R.**
"Synaptotagmin II negatively regulates Ca^{2+}-triggered exocytosis of lysosomes in mast cells".
J. Exp. Med. **189**, 1649-1658 (1999). (Immunology 5/115 IF 13.97)
40. Zussman, A. and **Sagi-Eisenberg, R.**
"Stimulation of Ca^{2+}-dependent exocytosis and release of arachidonic acid in cultured mast cells (RBL-2H3) by quercetin; Sensitization, linked to inhibition of Gi3 GTPase activity".
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41. Shefler, I. and **Sagi-Eisenberg, R.**
"Gi-mediated activation of the syk kinase by the receptor mimetic basic secretagogues of mast cells; role in mediating arachidonic acid/metabolites release.
J. Immunol. **167**, 475-481 (2001). (Immunology 12/115 IF 6.39)
42. Shefler, I. and **Sagi-Eisenberg, R.**
"Gi-mediated activation of the p42/p44 Mitogen-Activated Protein Kinases by receptor mimetic basic secretagogues is abrogated by inhibitors of endocytosis. International Immunopharmacology. **2**, 711-720 (2002). (Pharmacology 89/193 IF 2.0)
43. Baram, D., Peng, Z., Medalia, O., Mekori, Y.A. and **Sagi-Eisenberg, R.**
"Synaptotagmin II negatively regulates MHC class II presentation by mast cells". Molecular Immunol. **38**, 1347-1352 (2002). (immunology 19/115 IF 4.3).
44. Peng, Z., Grimberg, E. and **Sagi-Eisenberg, R.**
"Suppression of synaptotagmin II restrains phorbol ester-induced down-regulation of protein kinase Cα by diverting the kinase from a degradative pathway to the recycling endocytic compartment".
J. Cell Sci. **115**, 3083-3092 (2002). (Cell Biology 22/153 IF 6.54)
45. Grimberg, E., Peng, Z., Hammel, I. and **Sagi-Eisenberg, R.**
"Synaptotagmin III is a critical factor for the formation of the perinuclear endocytic recycling compartment and determination of secretory granules size."
J. Cell Sci. **116**, 145-154 (2003). (Cell Biology 22/153 IF 6.54)
46. Haberman, Y., Grimberg, E., Fukuda, M. and **Sagi-Eisenberg, R.**
"Synaptotagmin IX, a possible linker between the perinuclear endocytic recycling compartment and the microtubules".
J. Cell Sci. **116**, 4307-4318 (2003). (Cell Biology 22/153 IF 6.54)
47. Kapp Barnea, Y., Melnikov, S., Shefler, I., Jeromin, A. and **Sagi-Eisenberg, R.**
"Neuronal Calcium Sensor-1 (NCS-1) and phosphatidylinositol 4-kinase beta regulate IgE

receptor triggered exocytosis in cultured mast cells".
J. Immunol. **171,** 5320-5327 (2003). (Immunology 12/115 IF 6.39)
48. Atiya-Nasagi, Y., Cohen, H., Medalia, O., Fukuda, M. and **Sagi-Eisenberg, R.**
"O-glycosylation is essential for intracellular targeting of synaptotagmins I and II in non-neuronal specialized secretory cells".
J. Cell Sci. **118,** 1363-1372 (2005). (Cell Biology 22/153 IF 6.54)
49. Haberman, Y, Ziv I, Gorzalczany, Y, Fukuda, M and **Sagi-Eisenberg R.**
"Classical protein kinase C(s) regulates targeting of synaptotagmin IX to the endocytic recycling compartment".
J Cell Sci. **118,** 1641-1649. (2005). (Cell Biology 22/153 IF 6.54)
50. Kapp-Barnea, Y., Ninio-Many, L., Hirschberg, K., Fukuda, M., Jeromin, A. and **Sagi-Eisenberg, R.**
"Neuronal Calcium Sensor-1 (NCS-1) and PI4Kβ stimulate ERK1/2 signaling by accelerating recycling through the endocytic recycling compartment (ERC)."
MBC. **17,** 4130-4141 (2006). (Cell Biology 23/153 IF 6.52)
51. Haberman, Y., Ziv, I., Gorzalczany, Y., Hirschberg, K., Mittleman, L., Fukuda, M. and **Sagi-Eisenberg, R.**
"Synaptotagmin (Syt) IX is an essential determinant for protein sorting to secretory granules in mast cells ".
Blood. **109,** 3385-3392 (2007). (Hematology 2/60 IF 10.13)
52. Merimsky, O., Gorzalczany, Y. and **Sagi-Eisenberg, R.** "Molecular impacts of rapamycin based drug combinations; Characterization of the molecular consequences of applying the mTOR inhibitor rapamycin with either gemcitabine or imatinib mesylate on human leiomyosarcoma". Int. J. Oncology. Accepted. (Oncology 55/123 IF 3.16)
53. Shefler, I., Zavaro, O., Raz, T. Baram, D. and **Sagi-Eisenberg, R.**
"Inhibition of basic secretagogues-induced signaling in mast cells by cell permeable Gαi-derived peptides." Int. Arch. Allergy. Under revision. (Allergy 5/16 IF 2.2).

B. INVITED REVIEW ARTICLES IN JOURNALS

1. **Sagi-Eisenberg, R.** and Pecht, I.
"The dual role of protein kinase C in the stimulus-secretion coupling of basophils".
Rev Clin Basic Pharm 33S-37S (1985).
2. Aridor, M. and **Sagi-Eisenberg, R.**
"The role of GTP-binding proteins in the control of mast cell exocytosis".
Cellular and Cytokine Networks in Tissue Immunity 11, 169-175 (1991).
3. Baram, D. ,Mekori, Y.A. and **Sagi-Eisenberg, R.**
Synaptotagmin Regulates Mast Cell Functions.
International Arch. Allerg. Immunol 124: 166-168 (2001).
4. Baram, D., Mekori, Y.A. and **Sagi-Eisenberg, R.**
"Synaptotagmin Regulates Mast Cell Functions."
Immunol. Reviews. 179:25-34 (2001).
5. **Sagi-Eisenberg, R.**
"The Molecular Mechanisms of Allergic Diseases; IgE-Dependent and IgE-Independent Signaling Pathways Converge in Eliciting the Release of Arachidonic Acid Metabolites".
The Israel Medical Association Journal. 4: 963-966 (2002).

6. **Sagi-Eisenberg, R.**
"The mast cell: where endocytosis and regulated exocytosis meet"
Immunol. Reviews. 217:292-303 (2007).
7. Fukuda, M. and Sagi-Eisenberg, R.
"Confusion in the nomenclature of synaptotagmins V and IX: which is which?"
Calcium Binding Proteins. In press.

C. CHAPTERS IN BOOKS

1. Pecht, I., **Sagi-Eisenberg, R.** and Mazurek, N.
"Modulation of Calcium Ions Fluxes as Signals for Mast Cells and Basophils Degranulation".
In: Mobility and Recognition in Cell Biology eds. Sund, Veeger, Walter de Gryters Co., Berlin, New York, pp. 409-426 (1983).
2. Pecht, I. and **Sagi-Eisenberg, R.**
"Calcium Channels Formation and Modulation in Secreting Basophils and Mast Cells".
In: Calcium, Neuronal Function and Transmitter Release, eds. B. Katz and R. Rahamimoff Martinus Nijhoff Publish, Boston pp. 457-471 (1984).
3. **Sagi-Eisenberg, R.**
"The role of protein kinase C in histamine secretion: Implications for the mode of action of the anti-asthmatic drug cromolyn"
In: Current Topics in Pulmonary Pharmacology and Toxicology. Hollinger, M.A. ed., pp. 24-42 (1987).
4. **Sagi-Eisenberg, R.**, Traub, L.M., Gat-Yablonski, G. and Aridor, M.
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